

CLAIMS

What is claimed is:

1. A method of inhibiting fibrosis in a patient said
5 method comprising administering a therapeutically effective
amount of somatostatin or a somatostatin agonist to said
patient.
2. A method of claim 1, wherein said method comprises
administering a therapeutically effective amount of a
10 somatostatin agonist to said patient.
3. A method of claim 2, wherein said fibrosis is in
the kidney.
4. A method of claim 2, wherein said fibrosis is in
the lung.
- 15 5. A method of claim 2, wherein said fibrosis is in
the liver.
6. A method of claim 2, wherein said fibrosis is in
the skin.
7. A method of claim 2, wherein said fibrosis is
20 induced by chemotherapy.
8. A method of claim 2, wherein said somatostatin
agonist is administered parenterally.
9. A method of claim 8, wherein said somatostatin
agonist is administered in a sustained release formulation.
- 25 10. A method of claim 3, wherein said somatostatin
agonist is administered parenterally.
11. A method of claim 10, wherein said somatostatin
agonist is administered in a sustained release formulation.
12. A method of claim 4, wherein said somatostatin
30 agonist is administered parenterally.
13. A method of claim 12, wherein said somatostatin
agonist is administered in a sustained release formulation.
14. A method of claim 5, wherein said somatostatin
agonist is administered parenterally.

16. A method of claim 14, wherein said somatostatin agonist is administered in a sustained release formulation.

16. A method of claim 6, wherein said somatostatin agonist is administered parenterally.

5 17. A method of claim 2, wherein said somatostatin agonist is administered topically.

18. A method of claim 7, wherein said somatostatin agonist is administered parenterally.

10 19. A method of claim 18, wherein said somatostatin agonist is administered in a sustained release formulation.

20. A method according to claim 2 wherein the fibrosis is induced by radiation.

21. A method according to claim 3 wherein the fibrotic disorder in the kidney is glomerulonephritis.

15 22. A method according to claim 3 wherein the fibrotic disorder in the kidney is diabetic nephropathy.

23. A method according to claim 3 wherein the fibrotic disorder in the kidney is allograft rejection.

20 24. A method according to claim 3 wherein the fibrotic disorder in the kidney is HIV nephropathy.

25. A method according to claim 4 wherein the fibrotic disorder in the lung is idiopathic fibrosis.

26. A method according to claim 4 wherein the fibrotic disorder in the lung is autoimmune fibrosis.

25 27. A method according to claim 5 wherein the fibrotic disorder in the liver is cirrhosis.

28. A method according to claim 5 wherein the fibrotic disorder in the liver is veno-occlusive disease.

30 29. A method according to claim 6 wherein the fibrotic disorder in the skin is systemic sclerosis.

30. A method according to claim 6 wherein the fibrotic disorder in the skin is keloids.

31. A method according to claim 6 wherein the fibrotic disorder in the skin is scars.

32. A method according to claim 6 wherein the fibrotic disorder in the skin is eosinophilia-myalgia syndrome.

33. A method according to claim 2 wherein the fibrosis is of the central nervous system.

5 34. A method according to claim 33 wherein the fibrotic disorder is intraocular fibrosis.

35. A method according to claim 2 wherein the fibrosis is in bone or bone marrow.

10 36. A method according to claim 2 wherein the fibrosis is in the cardiovascular system.

37. A method according to claim 2 wherein the fibrosis is in an endocrine organ.

38. A method according to claim 2 wherein the fibrosis is in the gastrointestinal system.

15 39. A method according to claim 7 wherein the fibrosis induced by chemotherapy is in the kidney.

40. A method according to claim 7 wherein the fibrosis induced by chemotherapy is in the lung.

20 41. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the liver.

42. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the skin.

43. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is of the central nervous system.

25 44. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in bone or bone marrow.

45. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the cardiovascular system.

30 46. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in an endocrine organ.

47. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the gastrointestinal system.

48. A method according to claim 20 wherein the fibrosis induced by radiation is in the kidney.

49. A method according to claim 20 wherein the fibrosis induced by radiation is in the lung.

50. A method according to claim 20 wherein the fibrosis induced by the radiation is in the liver.

51. A method according to claim 20 wherein the fibrosis induced by the radiation is in the skin.

52. A method according to claim 20 wherein the fibrosis induced by the radiation is of the central nervous system.

53. A method according to claim 20 wherein the fibrosis induced by the radiation is in bone or bone marrow.

54. A method according to claim 20 wherein the fibrosis induced by the radiation is in the cardiovascular system.

55. A method according to claim 20 wherein the fibrosis induced by the radiation is in an endocrine organ.

56. A method according to claim 20 wherein the fibrosis induced by the radiation is in the gastrointestinal system.

57. A method according to claim 2 wherein the fibrosis is induced by a drug or a combination of drugs.

58. A method according to claim 2 wherein the fibrosis is induced by a disease state.

59. A method according to claim 2 wherein the fibrosis is induced by an environmental or an industrial factor.

60. A method according to claim 2 wherein the fibrosis is induced by an immune reaction.

61. A method of inhibiting overexpression of TGF- β which comprises administering to a subject an effective amount of somatostatin, somatostatin agonist or a pharmaceutically acceptable salt thereof.

62. A method according to claim 61 wherein a somatostatin agonist is administered.

63. A method according to claim 62 wherein the

somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1 than the other human somatostatin sub-type receptors.

64. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 2 than the other human somatostatin sub-type receptors.

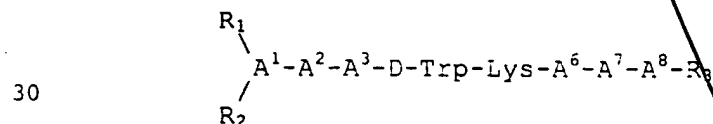
65. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 3 than the other human somatostatin sub-type receptors.

66. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 4 than the other human somatostatin sub-type receptors.

67. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 5 than the other human somatostatin sub-type receptors.

68. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin receptor sub-types 1, 2, 3, 4 and/or 5.

69. A method according to claim 62 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, β -Nal, β -Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe;

A² is Ala, Leu, Ile, Val, Nle, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A³ is pyridyl-Ala, Trp, Phe, β -Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A⁶ is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A⁷ is Ala, Leu, Ile, Val, Nle, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A⁸ is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe;

wherein X for each occurrence is independently selected from the group consisting of CH₃, Cl, Br, F, OH, OCH₃ and NO₂;

each R₁ and R₂, independently, is H, lower acyl or lower alkyl; and R₃ is OH or NH₂; provided that at least one of A¹ and A⁸ and one of A² and A⁷ must be an aromatic amino acid; and further provided that A¹, A², A⁷ and A⁸ cannot all be aromatic amino acids.

70. A method according to claim 62 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂; or

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala- β -D-Nal-NH₂ or a

pharmaceutically acceptable salt thereof.

71. A method according to claim 62 wherein the somatostatin agonist is

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys- β -Nal-NH₂;

-45-

- D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys- β -Nal-NH₂;
D- β -Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH₂;
D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH₂;
5 D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;
D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;
Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;
Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
10 H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
15 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Ac-D-Phe-Lys-Tyr-D-Trp-Lys-Val-Asp-Thr-NH₂, wherein an amide
bridge is between Lys and Asp;
Ac-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
20 Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-L-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
25 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
Ac-L-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH₂;
30 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;
Ac-hArg(CH₃, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-hArg(hexyl)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;

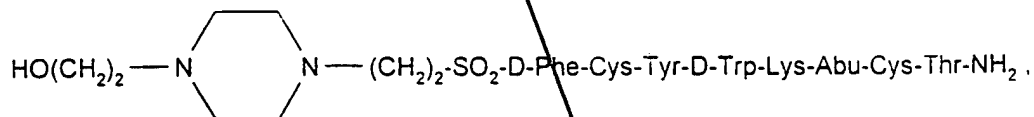
- cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);
5 cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
10 cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe);
15 cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-t-4-Amphe-Thr-Phe);
cyclo (Pro-Phe-D-Trp-t-4-Amphe-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-Amphe-Thr-Phe);
20 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba);
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH₂)₄CO);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-β-Ala);
25 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
30 cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp(NO₂)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);

cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba) ;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys) -OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys) -
 OH;
 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba) ;
 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba) ;
 cyclo (Phe-Phe-D-Trp(5F) -Lys-Thr-Phe-Phe-Gaba) ;
 cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac) -Thr-Phe-NH-(CH₂)₃-CO) ;
 cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
 cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba); or
 cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) or a
 pharmaceutically acceptable salt thereof.

72. A method according to claim 62 wherein the somatostatin agonist is D- β -Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂ or a pharmaceutically acceptable salt thereof.

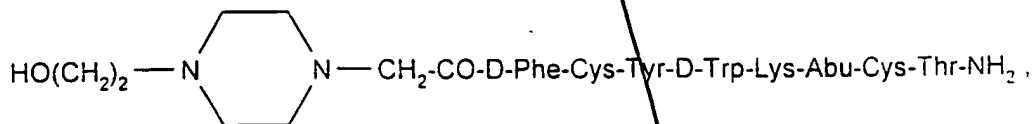
73. A method according to claim 62 wherein the somatostatin agonist is H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂ or a pharmaceutically acceptable salt thereof.

74. A method according to claim 62 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof.

75. A method according to claim 62 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof.

76. A method according to claim 62 wherein the somatostatin agonist is D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol or a pharmaceutically acceptable salt thereof.

77. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1 than the other human somatostatin sub-type receptors.

78. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 2 than the other human somatostatin sub-type receptors.

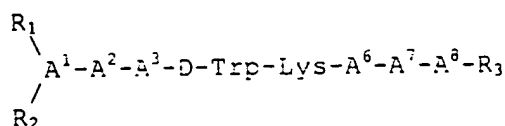
79. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 3 than the other human somatostatin sub-type receptors.

80. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 4 than the other human somatostatin sub-type receptors.

81. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 5 than the other human somatostatin sub-type receptors.

82. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin receptor sub-types 1, 2, 3, 4 and/or 5.

83. A method according to claim 2 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A¹ is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, β -Nal, β -Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A² is Ala, Leu, Ile, Val, Nle, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A³ is pyridyl-Ala, Trp, Phe, β -Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A⁶ is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A⁷ is Ala, Leu, Ile, Val, Nle, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A⁸ is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

wherein X for each occurrence is independently selected from the group consisting of CH₃, Cl, Br, F, OH, OCH₃, and NO₂;

each R₁ and R₂, independently, is H, lower acyl or lower alkyl; and R₃ is OH or NH₂, provided that at least one of A¹ and A⁸ and one of A² and A⁷ must be an aromatic amino acid; and further provided that A¹, A², A⁷ and A⁸ cannot all be aromatic amino acids.

84. A method according to claim 2 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂; or

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala- β -D-Nal-NH₂ or a pharmaceutically acceptable salt thereof.

85. A method according to claim 2 wherein the somatostatin agonist is

-51-

- D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys- β -Nal-NH₂;
D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys- β -Nal-NH₂;
D- β -Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH₂;
5 D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH₂;
D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;
D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;
Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;
10 Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
15 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Ac-D-Phe-Lys-Tyr-D-Trp-Lys-Val-Asp-Thr-NH₂, wherein an amide
bridge is between Lys and Asp;
20 Ac-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-L-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
25 Ac-D-hArg(CH₂CF₃)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
Ac-L-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
30 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;
Ac-hArg(CH₃, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-hArg(hexyl)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;

-52-

- Ac-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
Ac-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
Propionyl-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys (iPr)-Thr-Cys-Thr-NH₂;
- 5 Ac-D-β-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg (Et)₂-NH₂;
Ac-D-Lys (iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg (CH₂CF₃)₂-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg (CH₂CF₃)₂-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-
- 10 Cys-Phe-NH₂;
Ac-D-hArg (Et)₂-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH₂;
- 15 Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH₂;
Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH₂;
Bmp-Tyr-D-Trp-Lys-Val-Cys-D-Nal-NH₂;
H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
- 20 H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-β-Nal-NH₂;
H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Ac-D-β-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-β-Nal-NH₂;
- 25 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-β-Nal-NH₂;
H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
H-D-Phe-Cys-β-Nal-D-Trp-Lys-Val-Cys-Thr-NH₂;
- 30 H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH₂;
cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);

-53-

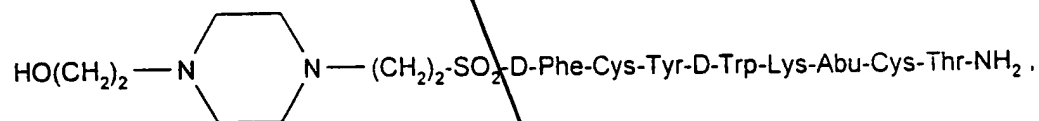
- cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);
5 cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe);
cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe);
10 cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
15 cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe);
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe);
cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe);
20 cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba);
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH₂)₄CO);
25 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-β-Ala);
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
30 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-D-Trp(NO₂)-Lys-Thr-Phe-Gaba);
cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);

- cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;
 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);
 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba);
 cyclo (Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba);
 cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-(CH₂)₃-CO);
 cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
 cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba); or
 cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) or a
 pharmaceutically acceptable salt thereof.

86. A method according to claim 2 wherein the somatostatin agonist is D-β-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂ or a pharmaceutically acceptable salt thereof.

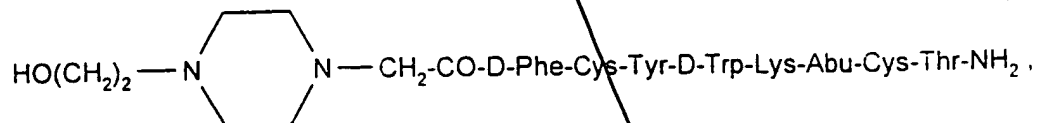
87. A method according to claim 2 wherein the somatostatin agonist is D-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂ or a pharmaceutically acceptable salt thereof.

88. A method according to claim 2 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof.

89. A method according to claim 2 wherein the somatostatin agonist is



-55-

or a pharmaceutically acceptable salt thereof.

90. A method according to claim 2 wherein the somatostatin agonist is D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol or a pharmaceutically acceptable salt thereof.

5 91. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the kidney.

92. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the lung.

10 93. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the liver.

94. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the skin.

15 95. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is of the central nervous system.

96. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in bone or bone marrow.

20 97. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the cardiovascular system.

98. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in an endocrine organ.

25 99. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the gastrointestinal system.

100. A method according to claim 58 wherein the fibrosis induced by a disease state is in the kidney.

30 101. A method according to claim 58 wherein the fibrosis induced by a disease state is in the lung.

102. A method according to claim 58 wherein the fibrosis induced by a disease state is in the liver

103. A method according to claim 58 wherein the fibrosis induced by a disease state is in the skin.

104. A method according to claim 58 wherein the fibrosis induced by a disease state is of the central nervous system.

5 105. A method according to claim 58 wherein the fibrosis induced by a disease state is in bone or bone marrow.

106. A method according to claim 58 wherein the fibrosis induced by a disease state is in the cardiovascular system.

10 107. A method according to claim 58 wherein the fibrosis induced by a disease state is in an endocrine organ.

108. A method according to claim 58 wherein the fibrosis induced by a disease state is in the gastrointestinal system.

15 109. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the kidney.

110. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the lung.

20 111. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the liver.

112. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the skin.

25 113. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is of the central nervous system.

30 114. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in bone or bone marrow.

115. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the cardiovascular system.

116. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in an endocrine organ.

117. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the gastrointestinal system.

118. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the kidney.

119. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the lung.

120. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the liver.

121. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the skin.

122. A method according to claim 60 wherein the fibrosis induced by an immune reaction is of the central nervous system.

123. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in bone or bone marrow.

124. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the cardiovascular system.

125. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in an endocrine organ.

126. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the gastrointestinal system.

127. A method according to claim 2 wherein the fibrosis is induced by a wound.

128. A method according to claim 127 wherein the fibrosis induced by a wound is in the kidney.

129. A method according to claim 127 wherein the fibrosis induced by a wound is in the lung.

130. A method according to claim 127 wherein the fibrosis induced by a wound is in the liver.

131. A method according to claim 127 wherein the fibrosis induced by a wound is in the skin.

5 132. A method according to claim 127 wherein the fibrosis induced by a wound is of the central nervous system.

133. A method according to claim 127 wherein the fibrosis induced by a wound is in bone or bone marrow.

10 134. A method according to claim 127 wherein the fibrosis induced by a wound is in the cardiovascular system.

135. A method according to claim 127 wherein the fibrosis induced by a wound is in an endocrine organ.

15 136. A method according to claim 127 wherein the fibrosis induced by a wound is in the gastrointestinal system.

137. A pharmaceutical composition useful for inhibiting fibrosis in a patient which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin, somatostatin agonist or a pharmaceutically acceptable salt thereof.

138. A pharmaceutical composition according to claim 137 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.

25 139. A pharmaceutical composition useful for inhibiting overexpression of TGF- β which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin, somatostatin agonist or a pharmaceutically acceptable salt thereof.

30 140. A pharmaceutical composition according to claim 139 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.

141. A method of claim 2, wherein said somatostatin agonist is administered orally.

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